IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Noritsugu Yamasaki et al. Art Unit: 1626

Serial No: 09/869,101 Examiner: Stockton, Laura

Filed: August 29, 2002

Title: BENZIMIDAZOLE DERIVATIVES

COMMISSIONER FOR PATENTS
Washington D.C. 20231

DECLARATION UNDER 37 C.F.R. § 1.132

1. I, Hiroshi Kayakiri, am a co-inventor of the above-identified U.S. patent application.

2. I am making this Declaration to provide relevant facts in support of the patentability of the subject matter claimed in the patent application.

3. I have read and understood the outstanding Office Action mailed on March 25, 2003.

4. I understand that the Examiner has rejected claims 1-6 under 35 U.S.C. §103(a) as being unpatentable over Yamasaki et al. (WO97/24334, U.S 6,166,219).

5. To demonstrate that the claimed compounds in this patent application have superior blood sugar decreasing activity to the prior art compounds, I submit experimental data, as described below.

6. Experimental data will be described hereafter, in which the experiment was conducted following Test Example of the specification (pages 107-109) of this patent application except that test compounds were orally administered and the following test compounds were used.

7. Test compounds used are compounds of Examples 13, 17, 22, 25, 44, 49, 53, 67, 70, and 73 of this patent application, and Compound 163 in Figure 21 on Sheet 21 of 58 and Compound 172 in Figure 22 on Sheet 22 of 58 of Yamasaki et al. Structures of these test compounds are shown in Test Results, attached hereto.

8. Animals used are five-week-old female mice [C57BL/KsJ-dbm db+/db+, C57BL/KsJ-dbm +m/+m (Jackson Laboratory)]. The mice were kept for 2 to 3 weeks and then used in the experiment.

9. The db/db mice were grouped according to the body weight and the plasma glucose concentration. Each test compound was administered at a dose, as indicated in Test Results

tubes (Chase Heparinized Capillary Tubes), and a plasma fraction was obtained through centrifugal separation. Plasma glucose concentration and the body weight were measured on day 0, day 7, and day 14. After the final collection of the blood, the mice were killed using CO_2 gas.

10. Immediately after the blood collection, the plasma glucose was measured by a glucose oxidase method (Glucose CII-Test Wako made by Wako Pure Chemical Industries, Ltd.) using from 10 to 15 μl of plasma.

11. The difference in the plasma glucose concentration between the control db/db mice and the +/+ mice was defined as 100%, and the rate (%) of decrease in the plasma glucose concentration of the group to which the test compound was administered was calculated as blood sugar decrease (%). The results are shown in Test Results, attached hereto.

12. The results reveal that the compounds of this patent application have superior blood sugar decrease activity compared to the compounds of Yamasaki et al.

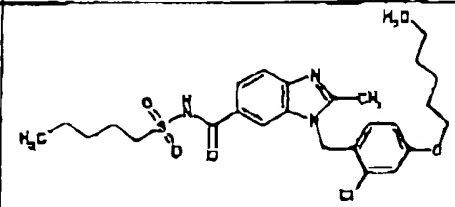
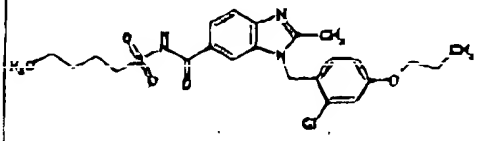
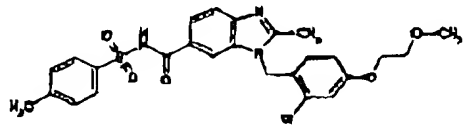
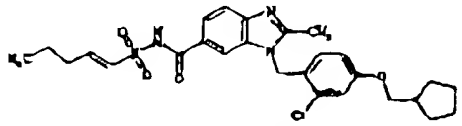
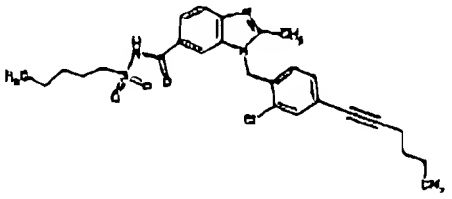
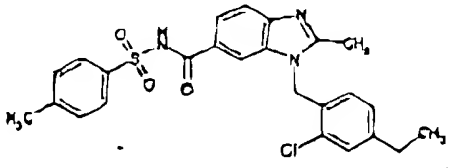
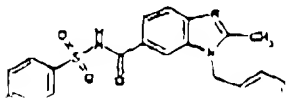
13. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. § 1001 and that such willful false statements may jeopardize the validity of any patent issuing from the present patent application.

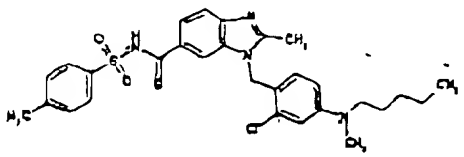
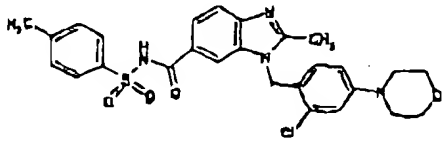
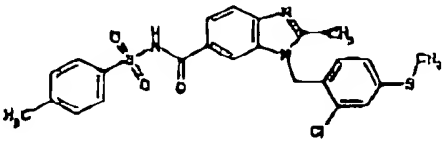
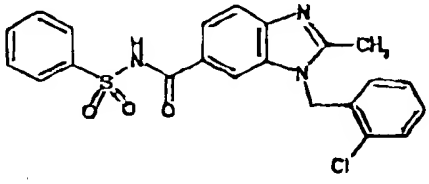
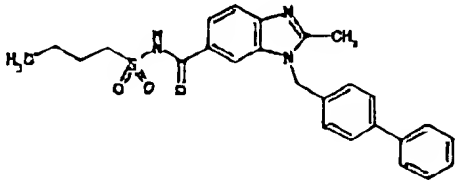
Sep. 22, 2003
Date

Kenichi Kayakiri

Test Results

Blood Sugar Level Depressing Activity in db/db mice

Test Compound	Structure	Dose (mg/kg)	Blood Sugar Decrease (%)
Example 13		1.0	48
Example 17		3.2 1.0	67 42
Example 22		1.0	33
Example 25		1.0	54
Example 44		1.0	46
Example 49		1.0	58
Example 53		1.0	49

Test Compound	Structure	Dose (mg/kg)	Blood Sugar Decrease (%)
Example 67		1.0	45
Example 70		1.0	40
Example 78		1.0	62
Compound (163) of Yamasaki et al.		30	17
Compound (172) of Yamasaki et al.		10 3	77 45